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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/922,227	08/02/2001	Erkki Ruoslahti	P-LJ 4859	7275
7590 11/26/2003				
CAMPBELL & FLORES LLP 4370 LA JOLLA VILLAGE DRIVE 7TH FLOOR SAN DIEGO, CA 92122			EXAMINER PRIEBE, SCOTT DAVID	
			ART UNIT 1632	PAPER NUMBER

DATE MAILED: 11/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.		Applicant(s)	
	09/922,227		RUOSLAHTI ET AL.	
	Examiner		Art Unit	
	Scott D. Priebe		1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 April 2003 and 29 September 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 and 6-17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 6-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The amendment filed 4/28/03 has been entered. Claims 4 and 5 have been cancelled. Claims 1 and 6 have been amended. Claims 7-17 have been added.

The terminal disclaimer filed on 9/29/03 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US Pat. Nos. 5,622,699; 6,068,829; 6,296,832; and 6,306,365 has been reviewed and is accepted. The terminal disclaimer has been recorded.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 8 and 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 8 and 16 recite that the library is “a library of diverse peptides and peptidomimetics” (emphasis added). Applicant points page 6, lines 24-28, of the specification for support. However, as acknowledged in the response, this teaches that the molecules or the library can be “peptides or peptide-like molecules” (emphasis added); the latter would include peptidomimetics. This does not teach administering a library including both peptides and peptidomimetics as recited in the new claims. There is no evidence that Applicant contemplated

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such an embodiment when the application was filed. This rejection would be overcome by replacing "and" with -- or --.

Claims 1-3 and 6 remain rejected and new claims 7-17 are rejected under 35 U.S.C. 112, first paragraph, for the reasons of record set forth in the Office action of 11/5/02, because the specification, while being enabling for methods using a library of diverse molecules, each molecule conjugated to a tag to provide recovery means and/or a polynucleotide tag that can be amplified by polymerase chain reaction to provide identification means, does not reasonably provide enablement for any other embodiment of the claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's arguments filed 4/28/03 have been fully considered but they are not persuasive. On page 12 of the response, point 1), Applicant refers to arguments made in application 09/227,906 alleging that the Examiner had acknowledged that one would be able to use recovered molecules that had homed to a particular organ without knowing their structure. In response, the arguments and/or evidence present in the parent application have not been made of record in this application. Also, the patented invention of the '206 application requires that the library members comprise a "tag" that is used to recover the library members from a particular organ. The key here is that if the library members can be recovered and isolated from an organ in sufficient quantity, then it is acknowledged that one could conceivably use them as a binding reagent, similar to polyclonal antisera. However, the instant claims do not require that the library members include such a tag.

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In point 2), Applicant asserts that arguments had been made previously concerning the scope of the compounds present in a library, and that the Examiner had acknowledged that preparation of various types of molecules for libraries would have been within the ability of one of skill in the art. In response, Applicant does not indicate where this argument was presented, it is not of record in the instant application. Also, the rejection does not indicate that the claims should be restricted to any particular classes of compounds in the libraries. Rather, mention is made of the lack of guidance for choosing libraries and for identifying or recovering members of such libraries from target organs commensurate in scope with the claims. It was discussed to emphasize the general lack of guidance in the specification and the need for the library molecules to comprise a tag used in recovery or in identification of the desired library members.

The relevance of point 3) to the rejection (page 13) is unclear. The rejection acknowledges does not indicate that the invention is enabled only for specific types of tag used for recovery. It only indicates that a tag providing means for recovering the molecules from the organ is required if a polynucleotide tag for identification is not present. The specification does not teach any tag other than a polynucleotide that can be used to identify library molecules present in a target organ.

In point 4) Applicant argues that the invention is enabled for libraries of untagged molecules. It is argued that the specification at page 8 teaches one to use HPLC to remove contaminating compounds, and that mass spectrometry and/or gas chromatography could be used to identify the structure of a homing molecule. Exhibits B, C, D and a declaration under R. 132 are alleged to provide support that one of skill in the art would know how to use such techniques to identify small organic molecules in organ or tissue samples. In response, the copies of exhibits

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B and C were of poor quality and most of the text could not be read. Exhibits B and C are alleged to relate to identification of metabolites of vitamin D2 tamoxifen, respectively. However, the purpose set forth in the instant application for molecules identified by the claimed method is to conjugate them to functional moieties to target those moieties to a target organ. The specification does not teach to make libraries including either of these types of compound nor that such compounds could be attached to moieties to target those moieties to a target organ, nor does it provide guidance as to how they would be identified in an organ sample. The declaration under 37 CFR 1.132 filed 4/28/03 is insufficient to overcome the rejection for the same reasons. The specification does not teach using libraries of benzodiazepines, attaching identified benzodiazepines to moieties to target them to an organ, nor how to identify specific benzodiazepine molecules in an organ. In addition, the declaration (para. 6) indicates that a pre-defined library of 10 different benzodiazepines was injected into mice, and identified in different organs by mass spectrometry. The specification does not teach to use predefined libraries. The quality of the figures is poor, and the specific molecular weights cannot be read for many of the peaks. With respect to Fig. 1, molecules 1B5 and 2C11 are each assigned to two different peaks. One peak appears at approximately the expected location for 1B5, however the second appears at that of a substantially higher MW. The declaration does not explain how it was determined that this second peak corresponded to 1B5, rather than 1B6 or 2C11, whose molecular weights are closer to that of this second peak. Also, neither of the peaks ascribed to 2C11 appear where expected for a molecule with the MW of 2C11. In Fig. 4, the peak ascribed to molecule 2E3 appears at a position that is closer to the MW of 1E4, than 2E3. The declaration does not explain how it was determined that the peak represented 2E3, rather than 1E4. Similarly, in Figs. 4 and 5

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the peak in each ascribed to 1B12 is at a position that would be closer to that expected for the MW of 1D6, 1B1 or 2D8 than to the MW of 1B12. Finally, Figs. 1 and 6 are purported to both be from brain, yet the spectra observed is different. This raises the question of whether the library had actually been administered to the mice, as stated in the declaration, or whether each compound had been administered to separate mice. The specification also does not teach to administer compounds individually to separate mice.

Exhibit D is purported to show that one would have known to have used a method involving 2-D protein electrophoresis and mass spectrometry to identify untagged peptides from a peptide library in the context of the invention. First, this paper was published shortly before the instant invention was made. Second, the specification neither mentions nor suggests using such a method, much less teaches how one would actually carry out such a method for identification of peptides from a library.

If there is no disclosure of starting materials and of conditions under which the process can be carried out, undue experimentation is required. Failure to provide such teachings cannot be rectified by asserting that the disclosure of the missing necessary information was well known in the prior art. See *Genentech Inc. v. Novo Nordisk A/S*, 42 USPQ2d 101, 1005 (CA FC, 1997). To comply with the enablement requirement, the disclosure in the application shall inform those skilled in the art how to use the invention, not how to find out for themselves how to use it. *In re Gardner*, 166 USPQ 138, 141 (CCPA 1970).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (703) 308-7310 (*-571-272-0733 after 1/12/04). The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Scott D. Priebe
Primary Examiner
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